SUPPORT FOR THE AMENDMENT

Claims 12-15 have been canceled.

No new matter has been entered by the present amendment.

REMARKS

Claims 1-11 and 16-20 are pending in the present application.

At the outset, Applicants wish to thank Examiner Carter and Examiner Padmanabhan for the helpful and courteous discussion with their undersigned Representative on August 23, 2007. During this discussion, several amendments and arguments were discussed to address the rejections of record. The content of this discussion is reflected in the amendments and remarks set forth herein. Reconsideration of the outstanding rejections is requested.

The rejections of: (a) Claims 1-5, 12, and 13 under 35 U.S.C. §103(a) over Nakajima et al in view of Georges et al, and (b) Claims 6, 7, 14, and 15 under 35 U.S.C. §103(a) over Nakajima et al in view of Georges et al and Ueda et al, are respectfully traversed.

The Examiner has taken the position that the claims are obvious over Nakajima et al (Exp. Cell Res. 1998) in view of Georges et al, with or without Ueda et al (J. of Antibotics, 1994). It is the Examiner's position that Nakajima et al disclose that FK228 is an inhibitor of intracellular histone deacetylase activity which strongly inhibits proliferation of tumor cells *in vitro* and greatly suppresses the growth of transplanted tumors in mice. However, the Examiner recognizes that Nakajima et al fail to specifically disclose the treatment of kidney cancer or suppression of a cancerous tumor in the kidney.

To compensate for this deficiency, the Examiner cites Georges et al. Georges et al discloses that an unrelated collection of compounds have been found to possess anti-cell-proliferation properties arising from their histone deacetylase inhibitory activity (see paragraph [0036]). Georges et al then concludes that due to the anti-cell-proliferation

properties, their compounds "are expected to be useful in the treatment of cancer... particularly in the treatment of cancers of the breast, lung, colon, rectum, stomach, prostate, bladder, pancreas, and ovary." Georges et al further speculate that "It is in addition expected that a derivative of the present invention will possess activity against a range of leukemias, lymphoid malignancies and solid tumors such as carcinomas and sarcomas in tissues such as the liver, kidney, prostate and pancreas" (see paragraph [0036]).

Using the HDAC inhibitory activity, the Examiner concludes that the treatment of cancer and/or suppression of cancerous tumors in the kidney would have been obvious to the skilled artisan. However, the Examiner is reminded that the legal standard for supporting a proper case of obviousness requires that three basic criteria be met: First, there must be some suggestion or motivation... to modify the reference... Second, there must be a reasonable expectation of success. Finally, the prior art reference... must teach or suggest all the claim limitations." (MPEP §2142) Applicants submit that the combined disclosures of Nakajima et al and Georges et al, with or without Ueda et al, fail to provide a reasonable expectation of success.

Specifically, from the cited sections above, Georges et al disclose that their compounds are "expected" to be useful in the treatment of a vast array of etiologically distinct cancers. No reasonable nexus or evidence is provided by Georges et al or the Examiner to show that the artisan would have a reasonable basis to expect that any HDAC inhibitor, including those disclosed in Georges et al as well as FK228, would be effective for treating any form of cancer from those recited. Thus, the statement in Georges et al can amount to nothing more that a wish or a hope, which at best offers an invitation to experiment. However, "obvious to try" has long been held *not* to constitute obviousness. *In re O'Farrell*, 7 USPQ2d 1673, 1680-81 (Fed. Cir.

1988). A general incentive (i.e., "a desire to enhance the production of 2'-deoxyribonucleosides") does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out. *In re Deuel*, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995).

To this end, Applicants wish to direct the Examiner's attention to page 2, lines 2-7, which provides a general view of the state of the art at the time of the present invention stating:

> As the situation stands, however, there are many problems yet to be solved, such as effectiveness of *in vitro* results in *in vivo* application, *in vivo* effectiveness against any tumor and the like. The antitumor activity *in vitro* against kidney cancer has been reported, but an antitumor activity *in vivo* against kidney cancer has not been reported.

Based on the foregoing, Applicants submit that there is no direct expectation of *in vivo* efficacy from the *in vitro* observation of HDAC inhibitory activity. This lack of expectation of success is clearly manifest in the combined disclosures of Nakajima et al and Georges et al. Thus, the claimed invention is not obvious in view of the combined disclosures of Nakajima et al and Georges et al.

During the discussion with the undersigned, the Examiner pointed to Ueda et al (J. of Antibotics, 1994) and alleged that this reference compensates for the deficiency in the combined disclosures of Nakajima et al and Georges et al. Specifically, the Examiner indicated that it is her position that this reference discloses the correlation between the observed *in vitro* effects to *in vivo* efficacy. The Examiner indicated that the basis for this position is the experiment bridging pages 303-304. However, Applicants respectfully submit that the cell lines used in this *in vivo* study are A549 and MCF-7, which are human ***lung*** adenocarcinoma and human ***mammary*** adenocarcinoma respectively. Further, the above-referenced text clearly states that these cells were transplanted ***under*** the kidney capsule of BDF1 mice. Thus, none

of these experiments provide any suggestion to ***treat kidney cancer*** or any expectation of the efficacy when so doing. Therefore, Ueda et al does nothing to compensate for the deficiency in the combined disclosures of Nakajima et al and Georges et al.

In view of the foregoing, Applicants request withdrawal of these grounds of rejection.

The rejections of Claims 12-15: (a) under 35 U.S.C. §101 and (b) under 35 U.S.C. §112, second paragraph, are obviated by amendment.

Claims 12-15 have been canceled. Accordingly, these grounds of rejection are moot.

Acknowledgment that these grounds of rejection have been withdrawn is requested.

Finally, Applicants respectfully request that the provisional obviousness-type double patenting rejections of: (a) Claims 1-7 and 12-15 over Claims 1-3 and 9 of co-pending application No. 11/064,292; (b) Claims 1-7 and 12-15 over Claims 60-62, 69, and 70 of co-pending application No. 10/948,288; and (c) Claims 1-7 and 12-15 over Claims 45 and 60 of co-pending application No. 10/486,833 in view of Georges et al, be held in abeyance until an indication of allowable subject matter in the present application. If necessary, a terminal disclaimer will be filed at that time. Until such a time, Applicants make no statement with respect to the propriety of this ground of rejection.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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